REMARKS

The enclosed amendments to the claims simplify issues for appeal. Entry is therefore requested.

Rejection under §101 and §112, first paragraph

Support for the claims 53-75 can be found in the specification e.g., as follows:

Claim 52: page 2, line 27 ("tracts"); page 3, line 4 ("unique"); page 29, lines 17-18 ("unique")

Claim 53: page 2, line 39

Claim 54: page 2, lines 26-27

Claim 55: page 4, lines 9-12

Claim 56: page 3, lines 7-9

Claim 57: page 23, line 35

Claim 58: page 2, line 27

Claim 59: page 1, line 5; page 2, line 26; page 2, line 34

Claim 60: page 2, line 43, 44 followed by page 3, lines 1-2

Claim 61: page 2, line 25 in combination with page 3, line 2

Claim 62: page 3, lines 5-6

Claim 63: page 3, line 10

Claim 64: page 2, lines 19-23

Claim 64(i): page, lines 25-29

Claim 64(ii): page 7, lines 1-3

Claim 65 (iii): page 4, lines 16-21

Claim 65(iv): page 4, lines 16-21

Claim 66: Example 2: page 29, lines 15-35, page 30, lines 17-24 and lines 5-15

Claim 67: page 30, lines 27-30

Claim 68: page 7, line 4

Claim 69: page 3, lines 13-15

Claim 70: page 3, line 15

Claim 71: page 2, lines 1-7

Claim 72: page 4, lines 16-21

Claim 73: page 2, lines 25-29 and line 34

Claim 74: page 2, lines 19-23

Claim 74(i): page 2, lines 25-29

Claim 74(ii) page 7, lines 1-3

Claim 74(iii): page 4, lines 16-21

Claim 74(iv): page 4, lines 16-21

Claim 74(v): page 6, line 34-41

Claims 64-74 are directed to methods of identifying a protein from a library of individual proteins that binds to a target of interest. The claimed method recites certain structural claimed aspects, including "protease sensitive sites" and "identifier sequence tracts which are unique" to the individual proteins in the library. The identifier sequence tracts can be used to recover ("identify") a protein in the library which has the desired binding characteristics after cleavage at the protease sensitive site. See, e.g., Claim 65(iv) and Claim 75(iv). The claimed method is generally useful for identifying proteins which are able to bind to targets of interest. As argued in the previous response: "The claimed library recites specific structural features which enable these methods to be carried out. In this respect, the library is no different than any other material which is used in molecular biology and protein chemistry."

In response to Applicant's previous arguments, it was stated in the Office action on Page 4: "The claims or the specification does not recite for any specific structure of the library." This is not correct. Claim 52 and others clearly recite specific structural features, e.g., "individual

identifier sequence amino acid tracts which are unique to said individual protein when bound to the specific target of interest, and are flanked by one or more protease sensitive sites ... " (Underlining added.) In Claims 65 and 74, e.g., these structures (i.e., identifiers and protease sensitive sites) are utilized to identify a protein with desired binding characteristics. This useful, novel, and unobvious method can be applied to many different kinds of proteins, including antibodies (e.g., Specification, Page 1, lines 12). The analogy to chromatography materials, fluorophores, and other reagents, argued in the previous Response (Page 14, Response dated April 12, 2004) related to the fact that these materials could be associated with other materials of any kind, just as the identifiers and protease sensitive sites can be joined to any desired library protein. A utility of the claimed invention involves the use of the identifiers and protease sensitive sites to select proteins with certain characteristics. The focus on the particular proteins to which the identifiers and protease sensitive sites are joined is misplaced, and the same reasoning would preclude any general method from being patented.

The reference to *Eli Lilly* and *Fiers* on Page 7 of the Office action is neither relevant nor appropriate. In those cases, the Applicant had discovered a single sequence for a protein from one mammalian species, but was attempting to cover the entire genus of mammalian proteins. This is not the case here. Applicant has claimed a general method of identifying proteins, and a library that is useful in this claimed method. Specific structural features are claimed. Applicant is not claiming beyond what is described and enabled in the specification, i.e., the general method and use of a library having certain structural features that make it useful in the method.

Claims of such type and scope have been granted by the Patent Office (e.g., System to detect protein-protein interactions, U.S. Pat Nos. 5,283,173; 5,468,617; and 5,667,973), as well as by the present examiner (e.g., "Method for preparing permuted, chimeric nucleic acid libraries," U.S. Pat. No. 6,322,969; "Methods of detecting interactions between proteins, peptides or libraries thereof using fusion proteins," U.S. Pat. No. 6,780,599). Applicant does not understand what is deficient in the specification for the pending claims. It is requested that the

Examiner specifically respond to this point so that Applicant may address it in continuing prosecution and/or appeals.

The allegation on Page 5 of the Office action that " ... there was no immediately apparent [sic] or 'real world' utility as of the filing date" is preposterous. Not only does the specification provide a number of uses of the claimed library and methods, but beginning on Page 26 of the Specification, several actual and working examples are described in which proteins with a binding affinity to a target were identified. This clearly is a substantial, specific, and credible utility.

Rejection under §112, second paragraph

A) It is stated that there is no positive recitation of the terms "tracts" and unique" in the Specification. As shown above, there terms are clearly utilized in the specification. (Nonetheless, this is not determinative, since there is no requirement for literal support of a claim term in the specification. The question more properly should focus on "possession" of the claimed invention.) As explained in the Specification, protein members of the library include "a tract of sequences (a 'barcode') which can subsequently be sequenced in order to identify which protein(s) has bound to the specific target ..." See, e.g., Specification, Page 2, lines 25-30.

It is also not clear why "one or more" is indefinite. One means "1" and "or more" indicates that the protein can comprise 2, 3, 4, etc., identifiers. Indeed, the examiner has allowed claims with such term (e.g., U.S. Pat. No. 6,194,544).

B) The term "adjacent" has its ordinary meaning. The sequence tracts are introduced adjacently prior to any association with another protein. Therefore, is not understood why the existence of "tertiary conformation" renders the term indefinite. Clarification is requested.

C) The term "introduced" has been canceled. This does not change the scope of the

claim, but simply removes the alleged indefiniteness to expedite prosecution.

D) Claim 71 has been amended to change its dependency.

Rejections under §102 and §103

There are numerous differences between the cited prior art and the subject matter recited in the claims. For example, it is stated on Page 10 of the Office action that Knappik (U.S. Pat. No. 6,300,064) describes a library with sequences "having **protease** cleavage sites." (Emphasis added.) The importance of the protease cleavage sites is described throughout the rejection. However, in fact, Knappik does not describe protease cleavage sites. They expressly define "cleavage site" at Column 14, lines 11-14 as being a DNA cleavage:

> Cleavage Site
> A short DNA sequence which is used as a specific target for a reagent which cleaves DNA in a sequence-specific manner (e.g. restriction endonucleases).

Absence this feature, the cited reference can not anticipate the claimed invention because it fails to disclose each and every claimed element. The rejections are therefore based on an incorrect understanding of the claimed invention and the cited prior art.

The addition of Ring (U.S. Pat. No. 5,849,877) and Markland (WO 92/15679) were sited for their teachings of specific protease cleavage sites. However, in view of the fact that Knappik does not teach using protease cleavage, there would have been no motivation coupled with an expectation of success to have modified the prior art to arrive at the present invention. To the contrary, Knappik expressly **teach away** from the modification urged in the Office action. For example, on Column 19, lines 17-20 of the Knappik patent, it is stated:

> In the case of Vl, a few amino acid exchanges were introduced in some of the chosen germline CDRs in order to avoid possible protease cleavage sites as well as possible structural constraints.

Thus, apparently where cleavage was possible, Knappik describe eliminating it.

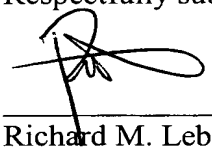
Furthermore, Ring describe proteolytic cleavage to yield free SFVs to obtain intact binding sites, not, e.g., to release identifier fragments. See, e.g., Ring, Column 34, line 65-Column 35, line 6. Compare, e.g., pending Claims 64, 65, and 74. Markland utilized cleavage sites, but to release phage. See, e.g., Summary of Invention, WO92/15679.

In view of these deficiencies, the addition of Hutchens simply for the teaching of MALDI-TOF, does not advance the rejection.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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